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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,559	10/27/2003	Robert F. Kaiko	200.1102CON3	2420

7590 07/26/2004

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EXAMINER	
TRAN, SUSAN T	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/694,559	KAIKO ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/06/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of applicant's Information Disclosure Statement, Preliminary Amendment filed 07/06/04, and Preliminary Amendment filed 10/27/03.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 and 11-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,277,384 ('384). Although the conflicting claims are not identical, they are not patentably distinct from each other because '384 claims an oral dosage form comprising an orally therapeutically effective dose of an opioid agonist, and an opioid antagonist, the dosage form having a ratio of opioid antagonist to opioid agonist that provides a combination product which is analgesically effective when the combination is administered orally, but which (i) is aversive in physically dependent human subjects when administered at the same dose or at a higher dose than said therapeutically

effective dose. The amount of antagonist included in the oral dosage form causes an aversive experience in a physically dependent addict taking about 2-3 times said therapeutically effective dose is found in claim 2. The opioid agonist is hydrocodone and the antagonist is naltrexone is found in claim 3. The opioid antagonist is naltrexone and the opioid agonist is oxycodone is found in claim 12. The opioid antagonist is naltrexone and the opioid agonist is codeine is found in claim 13. The weight ratios between the opioid agonist and opioid antagonist are found in claims 4, 5 and 12-20. Therefore, one of ordinary skill in the art would expect the same composition results from the use of the instant invention given the claims of '384. There are no unusual and/or unexpected results, which would rebut prima facie obvious. As such, the instant claims would have been obvious given the claims of '384, which set out a similar composition as claimed herein.

It is noted that there are number of applications appear to be potential double patenting based on overlapping, similar, or like subject matters. For example, 6,375,957; 6,696,066; 6,696,088; and 6,716,449. Therefore it is the applicants' obligation to submit terminal disclaimers for all applications requiring terminal disclaimers. The examiner puts applicants on notice, failure to comply with the requirement will result in a final rejection of the next office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 8, 12-14 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kreek US 4,769,372, in view of Dr. Medzon (Clinical Toxicology Review).

Kreek teaches an oral composition comprising combination of opioid analgesic and opioid antagonist (abstract, and column 5, lines 38-46). The opioid analgesics include hydrocodone, oxycodone, codeine, hydromorphone, meperidine, methadone, and morphine. Opioid analgesic is administered from 1 to 5 times daily in an amount of from about 1.5 to about 100 mg (column 3, lines 10-60; and column 4, lines 63 through column 5, lines 1-15). Suitable opioid antagonists include naloxone, naloxone glucuronide and nalmefene (column 3, lines 63 through column 4, lines 1-5; and column 4, lines 17-36). Opioid antagonist is administered in an amount of from about 1 to about 18 mg (column 5, lines 58 through column 6, lines 1-13). The weight ratio of opioid antagonist to opioid analgesic is at least 0.01:1, which would fall within the claimed ranges (calculated from 1 mg of opioid antagonist and 100 mg of opioid analgesic).

Kreek also teaches the oral dosage is in table, capsule, caplets, syrup, powder, elixirs and the like, with the use of carriers, binders, excipients, lubricants, disintegration agents, and sweeteners (column 5, lines 45-50).

Kreek does not teach naltrexone as an opioid antagonist.

Dr. Medzon teaches the use of naltrexone and nalmefene in place of naloxone for opioid detoxification (page 1, paragraphs 1, 2 and 5). Naltrexone is used in an amount of 50-100 mg daily (page 1, 3rd paragraph). Thus, it would have been obvious for one of ordinary skill in the art to modify the oral composition of Kreek using naltrexone as a suitable opioid antagonist, because Dr. Medzon teaches naltrexone by virtue of its' structural similarities to naloxone, shares the same properties exhibits by naloxone (page 1, 5th paragraph), because Dr. Medzon teaches naltrexone exhibits longer active opioid antagonists (page 1, 1st paragraph), and because Dr. Medzon teaches naltrexone has a high range of safety (page 3, 2nd paragraph). The expected result would be a dosage form comprising combination of opioid agonists and naltrexone suitable for oral administer that exhibits a low level of toxicity, low incidence of undesirable side effects, and low incidence of opioid abuse.

Claims 7, 10, 11 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kreek US 4,769,372, in view of Dr. Medzon (Clinical Toxicology Review) and Mitch et al. US 5,998,434.

Kreek and Dr. Medzon are relied upon for the reasons stated above. The references are silent as to the teachings of the additional non-opioid drug, as well as the

sustained release carrier. However, Mitch teaches oral dosage therapeutic combination of compounds to provide analgesic activity. The dosage form comprising combination of aspirin and codeine or other narcotic analgesics; combination of NSAID and muscarinic compound; or combination of one or more opioid compounds and selected muscarinic compound (column 1, lines 15-16; column 26, lines 65 through column 27, lines 1-22; column 28, lines 1-14; column 29, lines 13-24). Mitch also teaches opioid compounds include levorphanol (column 27, line 66). Mitch further teaches the oral dosage is in the form of tablet, capsule, sachet, or other container, with the use of conventional carrier, wetting agent, emulsifying agent, sweetening agent, and other additives to provide quick, sustained, or delayed release of the active ingredient (column 30, lines 38-64). Thus, it would have been obvious for one of ordinary skill in the art to modify the oral dosage form of Kreek using naltrexone of Dr. Medzon, in combination of other analgesic compounds in an oral dosage form in view of the teachings of Mitch, because Mitch teaches combination of analgesic compounds that is more effective to relieve pain with diminishing side effects and toxicity (column 1, lines 15-23), because Dr. Medzon teaches naltrexone exhibits longer active opioid antagonists (page 1, 1st paragraph), because Dr. Medzon teaches naltrexone has a high range of safety (page 3, 2nd paragraph), and because Kreek teaches oral dosage form that exhibits low level of toxicity and low incidence of undesirable side effects. The expected results would be a dosage form comprising combination of opioid analgesics and opioid antagonist compounds suitable for oral administration that is effective to relieve pain with low level of toxicity and diminish side effects.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kreek US 4,769,372, in view of Dr. Medzon (Clinical Toxicology Review) and FDA Consumer.

It is noted that the cited references do not teach the salt form of naltrexone, *e.g.*, naltrexone hydrochloride (HCl). However, it is well known in pharmaceutical art to use salt form of active compound. To be more significant, FDA Consumer is cited for the teaching of naltrexone HCl suitable for oral dosage form, *e.g.*, Revia® tablet (see abstract). Thus, it would have been obvious for one of ordinary skill in the art to modify the oral dosage form of Kreek using naltrexone and naltrexone HCl in view of the teachings of Dr. Medzon and FDA Consumer because Kreek teaches oral dosage form comprising combination of naloxone and opioid agonist that exhibits low level of toxicity and low incidence of undesirable side effects, because Dr. Medzon teaches naltrexone exhibits longer active opioid antagonists (page 1, 1st paragraph), because Dr. Medzon teaches naltrexone is approved by the FDA for use in alcohol detoxification (page 1, 2nd paragraph), and because FDA Consumer teaches the safety of using naltrexone HCl for treating alcoholism. The expected results would be a dosage form comprising combination of opioid analgesics and opioid antagonist compounds suitable for oral administration that has no toxicity and side effects.

Pertinent Arts

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. PR Newswire article, Boswell et al., Portoghese et al., Crain et

al., and Smith et al. are cited as of interest for the teachings of opioid agonist and/or opioid antagonist.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-R from 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached at (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Tran
Patent Examiner
AU 1615